

Indium-mediated allylation/propargylation of α -diazoketones: a facile synthesis of 1-bromo-2-alkyl- or 2-arylpent-4-en-2-ols

J. S. Yadav,* B. V. Subba Reddy, P. Vishnumurthy and Swapan Kr. Biswas

Division of Organic Chemistry, Indian Institute of Chemical Technology, Hyderabad 500 007, India

Received 23 April 2007; revised 11 July 2007; accepted 20 July 2007

Available online 27 July 2007

Abstract— α -Diazoketones undergo smooth allylation with successive bromide insertion with allylindium bromide generated in situ from allyl bromide and indium metal to produce 1-bromo-2-alkyl- or 2-arylpent-4-en-2-ols in high yields. Addition of propargylindium bromide produces 1-bromo-2-alkyl- or 2-arylpent-4-yn-2-ols under similar conditions.

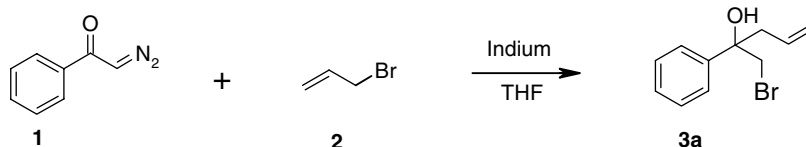
© 2007 Published by Elsevier Ltd.

α -Diazocarbonyl compounds find widespread applications in organic synthesis especially in natural product synthesis.¹ The ready availability and facile decomposition of α -diazocarbonyl compounds under thermal, photochemical, acid, base and transition metal catalysis conditions make them useful intermediates in organic synthesis.² Since the successful introduction of magnesium metal in Grignard reactions for carbon–carbon bond formation, the utilization of other metals of the periodic system for organic synthesis has received widespread attention and one of the recent additions is indium. Indium has emerged as a metal of high potential in organic synthesis because it possesses certain unique properties. Indium metal is unaffected by air or oxygen at ambient temperatures and can be handled safely without any apparent toxicity. In addition, indium exhibits low heterophilicity in organic reactions and thus oxygen- and nitrogen-containing functional groups are usually well tolerated by organoindium reagents.³ Moreover, indium-assisted reactions display low nucleophilicity thus permitting chemoselective transformations of

groups of similar reactivity.⁴ However, there have been no reports on the allylation of α -diazoketones using allylindium/propargylindium bromide.

In this report, we describe a novel and efficient protocol for the allylation/propargylation of α -diazoketones using allyl/propargyl bromide and indium metal. Initially, we attempted the allylation of diazoacetophenone (**1**) with allyl bromide (**2**) in the presence of indium metal. The reaction proceeded smoothly in THF at room temperature to produce 1-bromo-2-phenylpent-4-en-2-ol **3a** in 90% yield (Scheme 1).

A variety of α -diazoketones, such as *p*-methoxy-, *p*-methyl-, *p*-fluoro-, *o*-fluoro- and *p*-chlorophenyl derivatives, reacted efficiently with allylindium bromide to give the corresponding 1-bromo-2-aryl-pent-4-en-2-ols in satisfactory yields. Both aryl and alkyl substituted diazoketones worked well under the reaction conditions (Table 1). The *cis*-cyhalothric acid derived diazoketone gave similar results (Table 1, entry j). In addition, the

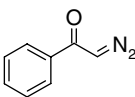

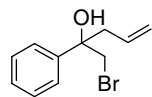
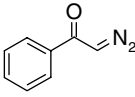

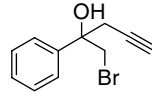
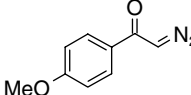

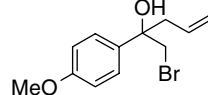
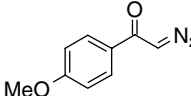

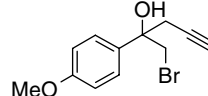
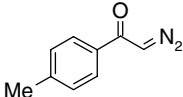

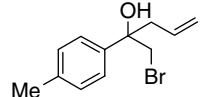
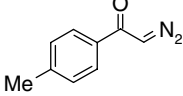

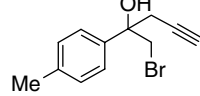
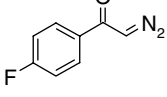

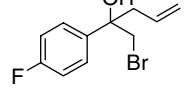
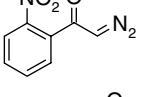

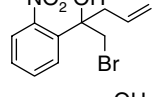
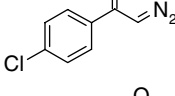

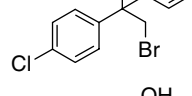
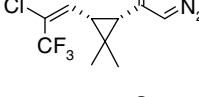

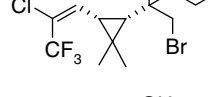
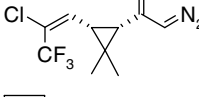

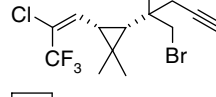
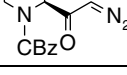

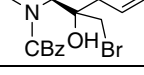


Scheme 1.

Keywords: Indium metal; α -Diazoketones; Bromo-insertion; Allylation/propargylation.

* Corresponding author. Tel.: +91 40 27193030; fax: +91 40 27160512; e-mail: yadavpub@iict.res.in

Table 1. Indium-mediated allylation/propargylation of α -diazoketones

Entry	α -Diazoketone	Allylbromide/propargyl bromide	Product ^a	Time (h)	Yield ^b (%)
a				46	90
b				51	82
c				42	75
d				44	70
e				45	80
f				48	72
g				46	89
h				47	87
i				45	90
j				46	79 ^c
k				48	71 ^c
l				45	90 ^c

^a Products were characterized by NMR, IR and mass spectroscopy.

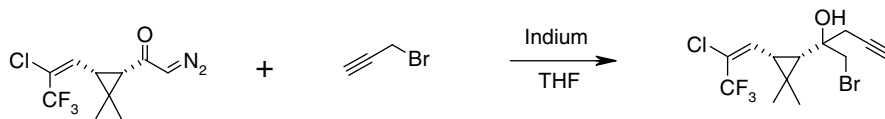
^b Yield refers to pure products after column chromatography.

^c Diastereomeric ratio of the crude product was 2:1 as confirmed by ¹H NMR spectroscopy.

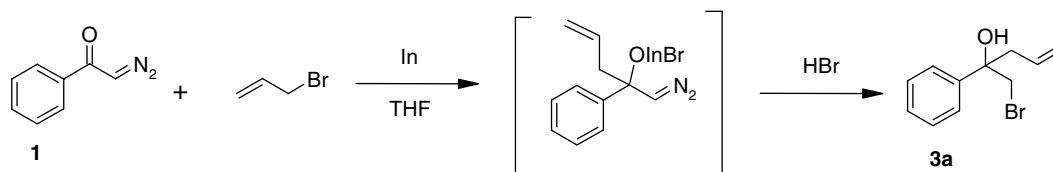
Cbz-protected L-proline derived diazoketone also underwent smooth allylation under the present conditions (Table 1, entry l). The method is clean and the products were obtained in high yields with high selectivity. No side products arising from Wolff rearrangement or carbene dimerization were observed under these conditions. As solvent, THF gave the best results over acetonitrile and dichloromethane. Activated zinc was also equally effective for this conversion. Similarly, α -diazoketones underwent propargylation with propargyl bromide un-

der identical conditions. For example, treatment of the *cis*-cyhalothric acid derived diazoketone with propargyl bromide in the presence of indium in THF gave the propargylated product in 71% yield (Table 1, entry k, Scheme 2).

In situ generated allyl/propargylindium bromide prepared from 1.2 equiv of indium and 1.5 equiv of allyl/propargyl bromide was effective for the allylation/propargylation of α -diazoketones.⁵ Mechanistically, it is pos-



Scheme 2.



Scheme 3. A possible reaction mechanism.

sible that allylation occurs initially, followed by decomposition of the allyl or propargyl diazo complex with HBr to afford the quaternary bromohydrin. A tentative reaction mechanism is shown in Scheme 3.

The scope of this method is illustrated with respect to various α -diazoketones and allyl/propargylindium bromide and the results are presented in Table 1.⁶

In conclusion, we have described an efficient protocol for the allylation/propargylation of α -diazoketones using allyl/propargyl bromide and indium metal. The use of indium makes this procedure quite simple and more convenient for scale-up. The products are potentially very useful precursors for the preparation of homoallyl epoxides, which are important building blocks in organic synthesis.

Acknowledgement

P.V.M. and S.K.B. thank the CSIR, New Delhi, for the award of fellowships.

References and notes

- (a) Padwa, A.; Weingarten, M. D. *Chem. Rev.* **1996**, *96*, 223–269; (b) Padwa, A. *Top. Curr. Chem.* **1997**, *189*, 121–269; (c) Calter, M. A. *Curr. Org. Chem.* **1997**, *1*, 37–70.
- (a) Doyale, M. P.; McKervey, M. A.; Ye, T. *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds from Cyclopropanes to Ylides*; Wiley-Interscience: New York, 1998; (b) Davis, H. M. L.; Hansen, T. J. *Am. Chem. Soc.* **1997**, *119*, 9075–9076.
- (a) Phil, H. L. *Bull. Korean Chem. Soc.* **2007**, *28*, 17–28; (b) Podlech, J.; Maier, T. C. *Synthesis* **2003**, 633–655; (c) Yadav, J. S.; Reddy, B. V. S.; Krishna, A. D.; Sadasiv, K.; Chary, Ch. J. *Chem. Lett.* **2003**, 248–249.
- (a) Ranu, B. C. *Eur. J. Org. Chem.* **2000**, 2347–2356; (b) Yadav, J. S.; Reddy, B. V. S.; Reddy, K. S.; Reddy, K. B. *Tetrahedron Lett.* **2002**, *43*, 1549–1551; (c) Yadav, J. S.; Bandyopadhyay, A.; Reddy, B. V. S. *Tetrahedron Lett.* **2001**, *42*, 6385–6388; (d) Yadav, J. S.; Anjaneyulu, S.; Moinuddin Ahmed, Md.; Subba Reddy, B. V. *Tetrahedron Lett.* **2001**, *42*, 2557–2559; (e) Yadav, J. S.; Bandyopadhyay, A.; Reddy, B. V. S. *Synlett* **2001**, 1608–1610.
- Yasuda, M.; Tsuchida, M.; Baba, A. *Chem. Commun.* **1998**, 563–564.
- General procedure:** A mixture of α -diazoketone (1 mmol), allyl bromide/propargyl bromide (1.5 mmol) and indium metal (1.2 mmol) was stirred in THF at room temperature for the appropriate time (Table 1). After complete conversion as indicated by TLC, the reaction mixture was quenched with aqueous saturated ammonium chloride (10 mL) and extracted with ethyl acetate (2 \times 10 mL). The combined organic extracts were dried over anhydrous Na₂SO₄, and concentrated in vacuo. The resulting product was purified by column chromatography on silica gel (Merck, 100–200 mesh, ethyl acetate–hexane) to afford the pure product. Products **3a**, **3c**, **3e**, **3h** and **3i** are reported in the literature.⁵ **Spectral data for selected products:** 1-Bromo-2-(4-methoxyphenyl)-4-pentyn-2-ol (**3d**): Liquid, IR (KBr): ν 3496, 2961, 2052, 1706, 1609, 1511, 1178, 695 cm⁻¹; ¹H NMR (200 MHz, CDCl₃): δ 7.98 (d, 2H, *J* = 8.4 Hz), 7.25 (d, 2H, *J* = 8.4 Hz), 3.98 (dd, 2H, *J* = 3.2, 11.0 Hz), 3.91 (s, 3H), 2.68 (s, 2H), 2.48 (s, 1H), 1.76 (br, 1H); ¹³C NMR (75 MHz, proton decoupled CDCl₃): δ 31.2, 41.8, 54.2, 74.4, 80.2, 84.7, 119.2, 126.9, 139.1, 158.8; EIMS: *m/z* (%): 272 (M+3), 271 (M+1), 187, 185, 152, 77, 64; CHN analysis for C₁₂H₁₃BrO₂, Calcd C, 53.55; H, 4.87. Found: C, 53.42; H, 4.95. 1-Bromo-2-(4-fluorophenyl)-4-penten-2-ol (**3g**): Liquid, IR (KBr): ν 3569, 3019, 2952, 1640, 1452, 1354, 1285, 1159, 865, 711 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 7.38 (t, 2H, *J* = 7.5 Hz), 7.01 (t, 2H, *J* = 7.5 Hz), 5.72–5.61 (m, 1H), 5.09 (t, 2H, *J* = 9.0 Hz), 3.92 (dd, 2H, *J* = 3.0, 11.2 Hz), 3.81 (br, 1H), 2.65 (d, 2H, *J* = 7.5 Hz), ¹³C NMR (75 MHz, proton decoupled CDCl₃): δ 43.2, 49.7, 74.5, 115.8, 119.8, 128.3, 134.9, 142.3, 162.4; LC-MSD-Trap-SL: *m/z*: 282 (M+23); CHN analysis for C₁₁H₁₂BrFO, Calcd C, 50.98; H, 4.66. Found: C, 51.07; H, 4.61. (2S)-1-bromo-2-(1S,3S)-3-[(*E*)-2-chloro-3,3,3-trifluoro-1-propenyl]-2,2-dimethyl-cyclopropyl-4-pentyn-2-ol (**3k**): Liquid, IR (KBr): ν 3456, 2924, 1729, 1591, 1447, 1263, 767 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 6.98 (d, 1H, *J* = 8.5 Hz), 3.63 (dd, 2H, *J* = 3.1, 11.2 Hz), 2.81 (br, 1H), 2.62 (s, 2H), 2.53 (s, 1H), 1.56 (m, 1H), 1.24 (m, 1H), 1.05 (s, 3H), 1.02 (s, 3H); EIMS: *m/z* (%): 361 (M+3), 267, 265, 221, 207, 73, 55; CHN analysis for C₁₃H₁₅ClBrF₃O, Calcd C, 43.41; H, 4.20. Found: C, 43.35; H, 4.28.